Exhibit L

Chapter 2

Physiology of Elite Young Female Athletes

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Abstract

The participation of girls in elite sport has increased exponentially over the past 30 years. Despite these increases a tradition for recruiting boys for exercise studies persists and our knowledge of the physiologic response to exercise in girls remains limited. Girls' physiology varies with age and maturation and is underpinned by a divergent hormonal milieu which begins early in foetal life. Sexual dimorphism underlies much of the physiologic response to exercise, and becomes most acute during adolescence when boys become taller, heavier, less fat and are more muscular than girls. Young girl athletes are not simply smaller, less muscular boys. The widening sex disparity in responses to exercise during puberty cannot always be accounted for by size. The woeful number of studies on girls and our prior inability to non-invasively study the complexity of the cellular metabolic response to exercise means an integrative understanding of girls' physiological responses to exercise remains elusive. Success in elite sport requires intense training, which for a long time was thought to cause disruption to normal growth and maturation. It would appear that exercise training, without other predisposing factors, is unlikely to cause aberrations to either growth or maturation. Nevertheless, there is clear evidence of a boundary between healthy and unhealthy levels of exertion when coupled with caloric limitation. Sports in which intense training is combined with the need for leanness may predispose girls to increased risk of skeletal and reproductive health problems, and ensuring risk is minimised should be a priority.   Copyright © 2011 S. Karger AG, Basel

The young female athlete is unique. She stands out from her peers, who show declining levels of physical activity from early puberty [1]. In comparison to boys, she remains under-represented in competitive sport [2]. This persists to Olympic level competition with 1,704 fewer women competing at the 2008 Beijing Olympics than men [3]. Moreover, there are fewer scientific data on physiologic issues associated with exercise in girls than in boys. Traditionally, boys have been recruited for exercise studies and a search of key databases shows that this persists with comparatively fewer articles investigating physiologic responses to exercise in girls. This preference for recruiting boys reflects social constraints which can be traced back to Victorian values surrounding women, exercise and health [4]. Central to the issue of women's involvement in sport was biology, bolstered by the idea that a woman's structural and functional ability was unable to tolerate strenuous exercise, presenting considerable risk to her reproductive health. Indeed, whether or not chronic training causes less than optimal structural and functional alterations in girls remains the topic of lively debate [5–8].

Sexual dimorphism does indeed underlie much of the physiological response to acute and chronic exercise, and although a myriad of factors have been shown to influence the development of sport performance [9], structural and functional capacity represent a significant contribution to the gender differences notable. Figure 1
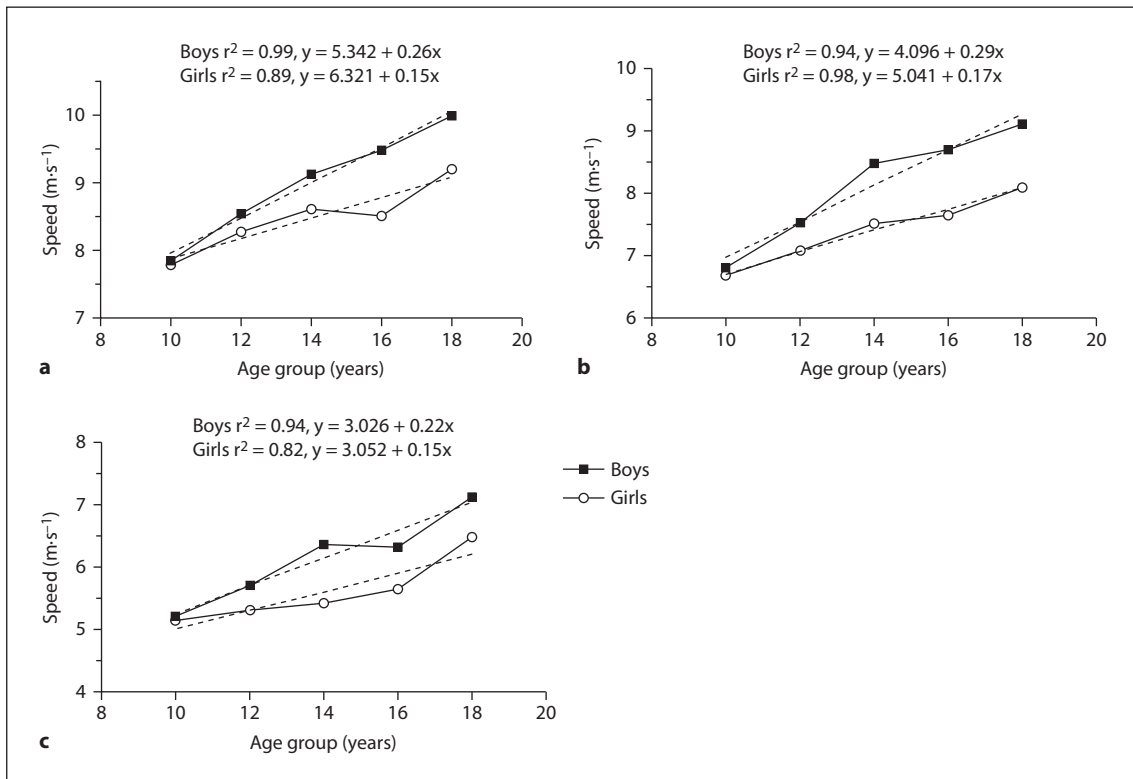
Fig. 1. Average running speed from North American age-group track and field records and world junior records over 100m (**a**), 400m (**b**) and 1,500m (**c**) for girls and boys.

illustrates the average running speed over 100, 400 and 1,500 m for girls and boys competing in age-group track and field championships in North America and world junior records [10, 11]. Analyses of these data show that regardless of distance, average running speed increases with age in both girls and boys ($r^2 > 0.82$ for all distances). Prior to 11 years of age differences in average speed are minimal, thereafter disparity becomes more pronounced with boys 8–15% faster than girls from 13 years of age onwards. This is consistent with the 9–15% advantage in speed adult men have over women across a wide range of distances from 100 m to 200 km [12]. When the slopes of the regression lines were compared between the sexes by age, these were significantly different for 100 and 400 m with the rate of improvement greater in the boys than the girls (see fig. 1). The rate of improvement in running speed over 1,500 m was similar between boys and girls with a pooled slope of 0.19. That an interaction between distance, speed developmental trajectories and sex exists suggests intriguing physiological mechanisms.

A key question to be addressed is whether the superior performances of boys relate to qualitative discrepancies in functional capacity or alternatively, they are simply a function of the increased body size and disparate body composition that accompanies adolescent growth and maturation. Appropriate adjustment for differences in body size and composition dampen many apparent

physiological differences [13, 14]; however, young girl athletes are not simply smaller, less muscular boys. Girls' physiology varies with age and is underpinned by a divergent hormonal milieu which begins early in foetal life. There is evidence that in the two-cell stage of embryonic development, long before visual gonadal differentiation, the sex-determining region of the Y chromosome has already been transcribed [15]. Testosterone secretion commences at about 3 months in the male foetus, the absence of which in the female foetus allows maturation of the female reproductive organs, and by birth subtle differences in cardiac function and body composition already exist [16, 17]. The accentuated hormonal adjustments which occur during adolescence result in differential development and a widening sex disparity in many physiological responses to exercise, some of which cannot be accounted for by size.

The primary focus of this chapter is on physiologic issues that are associated with exercise in girls; but to illustrate sexual dimorphism, comparisons will be made with boys where relevant. The chapter begins with a brief overview of growth and maturation in girls, including a discussion of issues related to body composition and size. This is followed by a focus on the acute responses to sustained aerobic exercise, as well as short-duration high-intensity exercise in girls. The possible physiological mechanisms that underlie these responses, such as sex differences in pulmonary, cardiac, and peripheral function, as well as cellular metabolism are discussed. The chapter concludes with consideration of the contention that intensive training poses a substantial threat to the development and health of young girls.

Growth and Maturation

Growth hormone (GH), insulin-like growth factor I (IGF-I), the sex steroids and insulin are all potent anabolic hormones. Their complex interactions enable linear growth, bone mineralization, increases in muscle and metabolic adaptations during childhood and adolescence and much of this hormonal mélange is sex dependent [18]. For example, the physiological effects of the sex steroids testosterone and oestrogen differ markedly, with evidence that combined testosterone and GH administration causes increases in IGF-I concentrations, resulting in enhanced anabolism, greater increases in fat free mass and higher whole body protein synthesis in boys [19]. Oestrogen administration, on the other hand, has been shown to have no effect on whole body protein synthesis in girls [19]. Sex dimorphic growth and development is most pronounced during adolescence, which forms the primary focus of the following sections.

Stature and body mass follow a double-sigmoid growth pattern in girls and boys, with rapid gains in infancy, slower yearly gains of about 5–6 cm in stature and 2.25–2.75 kg in body mass through childhood, and a second rapid gain in adolescence [20]. Girls usually begin adolescent growth before boys and progress at a faster rate than boys [21, 22]. At the peak of the adolescent growth spurt, girls gain approximately 8–9 cm in a year in stature. Boys only gain about 3 cm more in stature during the adolescent growth spurt, but are about 11–13 cm taller by adulthood because of their extra pre-adolescent growth [23]. From onset to completion, adolescent growth in stature lasts about 4–4.5 years in girls, until rising levels of oestrogen induce epiphyseal fusion marking an end to the growth in stature, usually around a skeletal age of 15 years [18, 21]. Peak body mass velocity is in lag by some 4–6 months with peak height velocity and total body mass gains of 16 kg are usual during the adolescent growth spurt in girls [24].

Other body proportions such as sitting height, leg length, biacromial and bicristal breadths follow a similar growth pattern to stature. Leg length and sitting height differ little between girls and boys during childhood [23]. At the onset of adolescence rapid growth in leg length precedes trunk growth. Boys surpass girls in leg length by about 12 years of age and in sitting height around

14 years of age. Yet, the ratio of sitting height to stature is higher in girls than boys through adolescence indicating relatively shorter legs in girls for the same stature. Girls have a marginally wider bicristal breadth than boys from late childhood to late adolescence, when boys catch-up [23]. In contrast, boys experience much more dramatic increases in biacromial breadth compared to girls [23]. When bicristal breadth is expressed as a ratio of biacromial breadth (hip-to-shoulder ratio), in comparison to boys values are higher in girls from early childhood, with bicristal breadth approximately 72–73% of biacromial breath, remaining quite stable through adolescence. In boys a decline in this ratio is noted from about 70% at 11 years of age, to 65% by 16 years of age, which is an outcome of the disproportionately faster growth of biacromial breadth [23]. Interestingly, although stature as well as mass-to-stature ratio differ between girls involved in different competitive sports, minimal differences in other proportions such as arm span and seated height have been reported [25, 26]. Greater mass-to-stature ratios can confer performance benefit in some sports such as throwing events; however, the combined effect of broader hips and shorter legs that usually accompany a greater mass-for-stature and characterize early maturation in girls, is generally disadvantageous. Although data are sparse, young female athletes in running events or gymnastics are generally more likely to be characterized by longer legs, lower hip-to-shoulder ratios and lower mass-for-stature.

Assessment of maturity stage is vital but poses considerable challenge. Skeletal age is the biological marker of choice, but is hindered by ethical constraints related to ionizing radiation exposure. The timing and tempo of sexual maturation in girls has most commonly been described using the visual descriptive stages of secondary sexual characteristics. These were first documented by Reynolds and Wines [27], and then further refined by J.M. Tanner and are better known as Tanner stages [28]. There is a large normal variation in the timing and tempo of sexual maturation in girls, as well as clearly documented sex differences. Like linear growth, girls normally begin sexual maturation before boys and progress toward full maturity at a faster tempo than boys [22].

A recent large-scale longitudinal study of Caucasian and African-American children suggests that the average girl begins breast development at 9.8 years, whilst the average boy begins genital development at about 10.3 years [21]. Pubic hair growth usually occurs around 10.2 years in girls and around 11.3 years in boys. The onset of the initial stages of sexual maturity in these American girls is somewhat earlier than previously published data for European girls, for whom breast budding was reported to occur at about 10.5 years and Tanner Stage two for pubic hair at 10.8 years [28, 29]. This discrepancy probably reflects the different racial mix of the groups, in addition to a possible secular trend for a declining age of onset of maturation [30].

Asynchronous maturation of secondary sex characteristics in girls is common and has been defined as a difference of at least 4 months between breast and pubic hair development. About 51–66% of girls follow an asynchronous maturation pattern [21, 31]. Most (about 70%) follow a thelarchal pathway, with breast development beginning prior to pubic hair growth (adrenarche). Asynchrony usually persists into Tanner stage 3, the onset of which is on average 11.3 years for breast development, with pubic hair stage three occurring some 2 months later [31]. As the latter stages of sexual maturity are attained, development becomes more synchronous. A minority of girls (approximately 30%) follow an adrenarchal asynchronous pathway, in which pubic hair development precedes breast development. Thelarchal asynchrony is believed to result from initial advanced stimulation of gonadotropin and oestrogen, thereby enabling earlier breast development. The converse is true of adrenarchal asynchrony, where the advanced production of testosterone and adrenal hormones promotes earlier pubic hair growth. Age of onset of menses usually

occurs during Tanner stage three for breast development. For those girls following the thelarchal pathway, menses occurs at an earlier age, around 12.6 years. Those following the adrenarchal pathway usually begin menses around 13.1 years [21, 31]. Lower oestrogen levels are noted in girls following an adrenarchal maturation pathway which persists throughout adolescence. This affords a body composition advantage, characterized by a lower sum of skinfolds, percent body fat and waist-to-hip ratio [31]. Girls involved in intensive training are generally characterized by lower percent body fat, but there is little evidence to suggest that they preferentially follow an asynchronous adrenarchal pathway [32].

The presence of asynchronous sexual maturation has implications when comparing young athletes with non-athletes, as well as making comparisons between girls and boys. Whether alignment is on the basis of a single marker (e.g. pubic hair development), the creation of a composite score for both pubic hair and breast development, or on differing secondary sex characteristics (such as genitalia and breast development), the assumption is that the timing of the appearance of a particular characteristic, as well as the tempo, is homogeneous. This is clearly not always the case, and it has been suggested that alignment of sexual maturation to other biological or somatic markers of maturation (e.g. age at menarche or peak height velocity) is more appropriate [33]. Menarchal age is convenient if retrospective, otherwise, like peak height velocity, a prospective research design is necessary. Assessment of maturational stage continues to present a real methodological challenge to paediatric exercise physiologists.

Body Composition and Size

Fat

Small sex differences in fat mass and percent body fat are evident from mid-childhood, with levels rising substantially in girls during adolescence. Body fat gains by the end of puberty usually result in 26–31% body fat in the average adolescent girl [34, 35]. Young athletes are generally leaner than the average non-athletic girl, but this is dependent on the chosen sport. Values as low as 14.3% have been reported for 15-year-old rhythmic gymnasts, with gymnasts generally showing lower body fat than other athletes [34]. Body fat values from 21 to 25% have been reported for dancers, distance runners and cross-country skiers from the ages of 10–17 years [36–39]. Higher values have been reported for 13- to 17-year-old high-school athletes competing in lacrosse, soccer, softball, swimming, track and field and volleyball (mean 27.4 ± 0.7%) [40].

Sex steroids are major determinants of body fat distribution, with the increases in body fat generally subcutaneous and in the gluteal and femoral regions in girls. Fat mass, combined with a smaller leg length-to-stature ratio, lowers the centre of gravity in girls, thereby affording better balance. However, fat mass is also negatively related to heat dissipation, which may prove disadvantageous in girls during endurance events in hot environmental conditions [41].

Fat tissue has relatively uniform properties throughout life, with negligible water content and a tissue density of 0.9007 kg$\cdot$l^{-1} [42]. Recent reference data from Wells et al. [42] have shown that in comparison lean tissue shows sex-specific chemical maturation, with decreases in water content and increases in density with increasing age. These new data have implications for the assessment of body fat since previous reference data extrapolated rather than directly assessed age specific tissue densities and hydration. Wells et al.'s [42] work provides the first comprehensive empirical data set for lean tissue properties for 4- to 23-year-old boys and girls, with lean tissue density values in girls of 1.0905 kg$\cdot$l^{-1} at 8–9 years, rising to 1.1021 kg$\cdot$l^{-1} at 16–17 years. Lean tissue hydration values declined with age from 75.2% at 8–9 years to 73.7% at 16–17 years

in girls. Importantly, this study has shown that these new values differ from previously simulated values. The lean tissue density values of Wells et al. [42] were consistently higher, whilst the hydration data were consistently lower than those reported by Lohman [43]. Comparisons of % fat calculated from densitometry with the Lohman [43] formula led to a between-study error of –1 to 2.5% fat in the average girl. Wells et al. [42] provide important new reference values for the assessment of body fat by both hydrometry (total body water, bioelectrical impedance) and densitometry which should ensure greater clarity in future analyses.

Muscle

At birth, boys tend to have a greater lean mass than girls. This difference remains small but detectable throughout childhood with about a 10% greater lean mass in boys than girls prior to puberty [17]. The sharp increase in muscle mass disparity between the sexes during puberty indicates a primary role of the gonadal steroidal hormones. Muscle mass in girls increases from about 25 kg at 10 years of age to about 45 kg by 18 years of age [42]. Reported values for 15- to 17-year-old female athletes are not dissimilar, ranging from 42 to 53 kg [23]. These gains in muscle tissue represent an increase of about 5% in muscle mass. The relative contribution of muscle mass to total body mass usually declines once consideration is given to the relative contribution of fat mass. In comparison, the androgen-mediated growth of muscle in boys results in muscle mass reaching about 55% of total body mass at maturity [44]. The greater overall skeletal muscle mass in adolescent boys creates a potential cascade of functional differences apparent in adults such as differing muscle fibre size, activities of metabolic enzymes, lipid content and oxidation, relative expression of myosin isoforms, and fatigability [45–50]. Maturation of these features remains poorly understood.

The use of ultrasonography and magnetic resonance imaging (MRI) are providing insight into changes in muscle architecture with growth. A recent study using ultrasonography demonstrated that muscle thickness (a marker of physiological cross-sectional area) and pennation angle were correlated with age from 4 to 10 years in both sexes [51]. Findings from MRI studies have shown similarly that muscle cross-sectional area increases with age from childhood through adolescence, and more so in boys than girls [52]. Pennation angle on the other hand has not been found to differ between the sexes [51]. Whilst muscle cross-sectional area and pennation angle are related to age, this has not been shown in muscle fibre length [51]. Muscle fibre length has been found to have high inter- and intra-individual variation, which may reflect a greater malleability in response to external stimuli such as the extent and intensity of exercise [51].

Morphological change in the muscle impacts upon function. Maximal strength, for example, is dependent on the specific joint angle (force-length relationship), contraction type, muscle cross-sectional area and velocity. The length of the muscle fibre is proportional to the absolute maximum contraction velocity, whilst the pennation angle dictates the proportion of force transmitted to the tendon. Muscle strength, expressed as torque, increases with age in children, but gains are greater in boys. This has been presumed to be an outcome of the greater muscle cross-sectional area [53]. Alternatively, there may be intrinsic sex differences in the fibre composition and fatigue characteristics of skeletal muscle that materialize during adolescence that also influence the ability to increase torque.

In adults, several studies have reported higher glycolytic enzyme activity and lower oxidative enzyme activity in men compared to women, supporting the contention that men have a lower proportion of type I fibres [50, 54]. Data on muscle fibre typing in children are limited because of the invasive nature of the biopsy methodology,

but there is evidence to show that differentiation of fibre type occurs during the first few years of life. About 10% of skeletal muscle fibres remain undifferentiated up until puberty, with no sex difference notable in the percentage of type I fibres (slow-twitch oxidative fibres) during childhood [55]. By adolescence females have a lower % of type I muscle fibres than males [45, 56] and the type II muscle fibres of young men are bigger than their type I fibres, something not evident in young women [56, 58].

Although boys gain more in strength than girls during adolescence, elite girl athletes are stronger than their less athletic peers. For example, average quadriceps and biceps isometric strength was reported to be 22% greater in elite gymnasts and swimmers and 18% greater in tennis players compared to less athletic school children [59]. Interestingly this study found no differences in strength between sports in the girls, even when co-varied for body mass. The relationship between strength and body mass, or strength-to-mass ratio, has been seen as an important predictor of sport performance particularly in gymnastics, middle- and long-distance running. Indeed, elite adult women runners such as Yvonne Murray and Greta Waitz were 17–18% below the average body mass for their stature at the peak of their running careers, which suggests relative strength was high. The work of Bencke et al. [60] has shown that 11-year-old girl gymnasts were the smallest, lightest and possessed the highest explosive strength compared to other athletes, suggesting high relative strength confers advantage in some sports in girls.

Bone

Bone characteristics differ little between boys and girls prior to puberty, but then follow two sex-divergent growth paths. During the adolescent growth spurt boys experience increases predominantly in bone diameter and cortical thickness due to periosteal apposition [17]. Girls on the other hand experience increases in cortical thickness, a decrease in medullary diameter, and little increase in periosteal diameter as a result of oestrogen inhibition of periosteal apposition [17, 61]. It should be noted that bone accretion and endocortical features appear to be site specific with data showing endocortical resorption at the mid-femur and proximal tibia in girls through puberty, but no endocortical resorption at the radial diaphysis [62, 63].

During puberty, bone mineral content (BMC) accrual rate is in lag with muscle accrual rate, suggesting that muscle enlargement, and concomitant increases in muscle force, are important for bone development [64]. Indeed, the 'functional muscle-bone unit' hypothesis suggests muscle force is a primary determinant of bone mass, structure and strength [65]. Young female runners and gymnasts have been shown to have elevated bone mass and enlarged bone size at specific sites such as the radius and lumbar spine in gymnasts [66] and the femur in runners [67], reflecting the specific mechanical-loading patterns these sports require. This has led some to conclude that muscular force alone explains the impact loading effect on bone [68–70]. On the contrary, recent research has shown that bone mass, size and strength increases in the upper extremity in gymnasts are independent of maturation, stature and muscle cross-sectional area and substantiates the hypothesis that other non-muscular loading factors may also account for skeletal adaptations [71, 72].

Puberty is the most favourable period for augmented bone mineralization, with about one quarter of adult bone being laid down. Bone mineral accrual is sex and maturity dependent and appears to be enhanced by oestrogen. It is clear that the early pubertal and pre-menarchal years are particularly important for young girls in terms of optimizing their bone mineralization and weight-bearing exercise plays a key complementary role in this process [73].

Body Size Considerations

By the time the adolescent growth spurt is complete the body size, shape and composition of boys and girls is different. Boys have become taller, have longer legs, broader shoulders, are heavier, and have less fat and more muscle than girls. The effect of these discrepancies on performance is substantial, and it is important in understanding girls' physiologic responses to exercise that we are able to effectively partition the impact of size from function. Traditionally in exercise physiology this has been achieved by expressing the physiological measure of interest (y) as a ratio of an appropriate marker of body size (x) to give the ratio y/x. Tanner suggested in 1949 that the use of such ratio standards to scale physiological measurements to size was 'theoretically fallacious and unless in exceptional circumstances, misleading' [74]. Yet this has largely been ignored with much of the comparison between men and women, or boys and girls based on ratio standards [75, 76]. An implicit assumption with the ratio standard is that the relationship is linear and the y intercept is zero. Additionally, ratio standards should only be used when the coefficient of variation (V) for body size (x), divided by the coefficient of variation (V) for the physiological variable (y), equals the Pearson product moment correlation coefficient (r) for the two variables, expressed by the equation V_x/V_y = rx,y. These assumptions are rarely met and the outcome is scaling distortion, which may have obscured our understanding of the physiologic responses of girls [77].

Theoretically, morphological and physiological variables are scaled according to the general allometric equation $y = ax^b$, where y is the morphological or physiological variable of interest, x is the chosen size denominator, *b* is the scaling exponent and *a* is the constant [78]. When this equation is solved the resultant power function ratio (y/x^b) is derived. Various studies have shown that with careful consideration of the denominator, alternative approaches, such as the allometric power function ratio or more complex multilevel modelling of longitudinal data, are more appropriate than ratio scaling when comparisons of various physiological outcomes between individuals of differing body size are sought [79, 80]. These alternatives should, wherever possible, be utilised.

Acute Responses to Aerobic Exercise

Peak oxygen uptake (peak $\dot{V}O_2$), the highest $\dot{V}O_2$ elicited during an exercise test to exhaustion in children, is well-established as the best single measure of aerobic fitness [81]. In comparison to boys, girls are characterised with a smaller absolute peak $\dot{V}O_2$. Predicted values range from 1.5 to 2.2 litres $\bullet$ min^{-1} in 10- to 16-year-old girls and are lower than boys by 11, 19, 23 and 27% at ages 10, 12, 14 and 16 years of age, respectively [82]. Peak $\dot{V}O_2$ is strongly correlated with body size and composition and thus, much of the divergence in values reflects this. When expressed as a ratio standard with body mass (ml $\bullet$ kg^{-1} $\bullet$ min^{-1}), peak $\dot{V}O_2$ shows a progressive decline in girls from 13 years of age, with values dropping from approximately 45 to 35 ml $\bullet$ kg^{-1} $\bullet$ min^{-1} [83]. In contrast, mass-related peak $\dot{V}O_2$ in young female runners has been found to be relatively constant with values of 56.3, 57.1, 56.9 and 54.3 ml $\bullet$ kg^{-1}$\cdot$min^{-1} at ages 10, 12, 14 and 16 years, respectively [84]. Likewise, peak $\dot{V}O_2$ has been shown to be fairly stable between 11 and 16 years of age in elite girl swimmers and tennis players [85], with values of 51–52 ml $\bullet$ kg^{-1} $\bullet$ min^{-1} and 47–49 ml $\bullet$ kg^{-1} $\bullet$ min^{-1}, respectively. When multilevel modelling was used to account for mass, stature and biological age, the elite girl swimmers and tennis players showed increases in peak $\dot{V}O_2$ until late puberty when increases became non-significant [85]. Similarly, in the less athletic population when more appropriate allometric adjustment is used to partition size effects in body mass and stature, peak $\dot{V}O_2$ has been found to increase significantly from 11 to 13

years in girls, and then remain constant with no decline into adulthood evident [81].

Dramatic pubertal changes in muscle, fat and mass contribute to the widening of the sex difference in peak $\dot{V}O_2$. When a marker of body fat was included in a multilevel regression model which incorporated body mass, stature and age, the sex difference in peak $\dot{V}O_2$ was reduced, but the greater increase in boys' peak $\dot{V}O_2$ with growth compared to girls was still not fully explained [83]. Equally, longitudinal data have shown that even when differences in body mass and fat mass are controlled for allometrically, girls utilise less oxygen than boys during submaximal exercise, and this becomes more pronounced with age [86]. Understanding the physiologic mechanisms that underlie these size-independent sex differences in peak and submaximal $\dot{V}O_2$ requires consideration of the coordinated systems response, which includes pulmonary, cardiac and peripheral adjustments to the demands in muscular energy. A discussion of key features of each follows.

Pulmonary

It was generally assumed that because exercise training exerts little influence on lung structure or function that the lungs exert minimal influence on oxygen transport. However, there is evidence that lung function adaptation does occur as a consequence of exercise training in girls [87]. Moreover recent investigation of sex differences in pulmonary structure and function in adults has shown considerable effects on gas exchange and the integrated ventilatory response during exercise, in particular exercise-induced arterial hypoxia [88]. There are well-documented sex differences in anatomical aspects of the pulmonary system which occur during lung growth [89]. The consequence of sex dependent pubertal thoracic growth is a larger thoracic width in boys. When coupled with a greater muscle mass for generating lower lung function, boys have approximately 25% greater lung volumes than girls

who are matched for stature [89]. By adult life, in addition to the smaller lung volumes, stature and age independent lower resting diffusion capacity (corrected for haemoglobin), lower maximal expiratory flow rates [90], and a greater occurrence of exercise-induced hypoxia has been shown in women [91]. Equally, there is also evidence that when matched for size and aerobic power women do not have reduced diffusion capacity or impaired ventilation perfusion during exercise [92].

In children, like adults, exercise pulmonary gas exchange depends on pulmonary ventilation ($\dot{V}_E$) and at maximal work rates high rates of ventilation are usual. Maximal values of 49–95 litres $\bullet$ min^{-1} have been recorded for girls between the ages of 9 and 16 years [93] and there is a consistent sex difference with values somewhat higher in boys (58–105 litres $\bullet$ min^{-1}) for the same age span. It should be noted that cross-study comparisons are difficult given the dependence of ventilation on the protocol and data such as these need to be interpreted cautiously. Maximum ventilation remains higher in boys, whether controlled for body size using a ratio standard or allometric adjustment with either stature and/or body mass [94, 95]. Thus, the higher peak $\dot{V}O_2$ in boys is indeed supported by a higher $\dot{V}_E$.

During exercise, an expiratory flow limitation is apparent in adult women but not men, resulting in a greater oxygen cost of breathing and the onset of arterial desaturation [88, 96]. Recent evidence has provided a comparison between pre-pubertal boys and girls and found no difference in the occurrence or severity of expiratory flow limitation between girls and boys and no changes in arterial saturation during exercise to maximum [97]. Others have found little evidence of exercise induced arterial hypoxaemia in pre-pubertal girls, or lower ventilatory efficiency at maximum [98, 99]. When Armstrong et al. [94] compared ventilatory parameters during submaximal exercise at the same absolute intensities they noted that girls demonstrated higher ventilatory equivalents for oxygen and carbon dioxide, i.e. poorer ventilatory

efficiency in comparison to boys. However, when they compared submaximal ventilatory efficiency during the same relative exercise intensities, values were remarkably similar between the sexes. This suggests that differences apparent at absolute submaximal exercise intensities simply reflect the higher relative percentage of maximum that girls are working at and do not denote true inefficiency.

There is little evidence that prior to puberty pulmonary structure or function limits oxygen uptake, however, considerable evidence has shown pulmonary function influences gas exchange in adult women, suggesting that maturational adjustments occur. At present however, there is little evidence to substantiate this.

Blood Volume and Haemoglobin

Assessment of blood volume in children and adolescents is complex and the variability in techniques means there are considerable discrepancies between studies. There are conflicting results regarding changes in blood volume with age. Some have shown that blood volume per unit body mass increases with age [100], others have found no change [101], whilst others report decreasing blood volume with age [102]. Likewise, data on sex differences in blood volume between girls and boys are mixed. When normalised using a ratio standard with body mass, differences between girls and boys were apparent from about 6 years of age, with values lower in the girls [103]. In contrast, when normalised using a ratio standard for lean body mass, sex differences are no longer apparent for pre-pubertal children, or at any maturational stage [103].

In boys, haemoglobin rises through adolescence to about 152 $g \bullet l^{-1}$ by 16 years of age [104]. Girls, on the other hand, usually demonstrate a plateau in haemoglobin concentration with values of about 137 $g \bullet l^{-1}$ by 16 years of age [104]. Highly trained adolescent female athletes also show lower haemoglobin concentration values compared to trained boys, with about a 7% difference [105]. Fully saturated, 1 g of haemoglobin carries 1.34 ml of oxygen, and one would presume that the smaller increase in haemoglobin in girls would result in a reduced oxygen carrying capacity in comparison to boys. However, it has been shown that haemoglobin concentration is not a significant predictor of peak $\dot{V}O_2$ in 11- to 17-year-olds once body size and composition and maturation have been controlled for [83].

Cardiac and Vascular Considerations

There are clear differences in cardiac function at rest and during exercise between girls and boys, with differences apparent even prior to puberty. The electrical conduction system is influenced by sex steroid hormones, with girls normally having higher resting heart rates than boys – somewhere in the magnitude of 90 beats per minute at around 10–12 years of age [106]. This is thought to relate to intrinsic differences in the sinus node pacemaker [107], a difference notable at birth with newborn boys displaying lower baseline heart rates than girls [16]. The higher resting heart rate in girls is often explained as an artefact of differences in cardiac dimensions, and indeed the ratio of heart mass to body mass has been found to be higher in boys than girls at birth, remaining so through adolescence [106]. Heart volume has also been found to be greater in boys with values of 342 and 403 ml for pre-pubertal girls and boys, respectively, and of 466 and 561 ml for pubertal girls and boys, respectively [108]. When adjusted for body mass these differences were found to persist through puberty (female 10.0 $ml \bullet kg^{-1}$; male 10.8 $ml \bullet kg^{-1}$). Inconsistencies in the findings, however, are present and others have found no differences in either left ventricular mass [109] or heart volume [110].

Echocardiographic studies that have shown greater left ventricular mass in boys compared

Table 1. Oxygen uptake, stroke index, cardiac index and arteriovenous oxygen difference at maximal cycle ergometer exercise

Reference	Sex	n	Age (years)	SI (ml$\cdot$m^{-2})	HR (bpm)	CI (litres$\cdot$ min$^{-1}\cdot$m^{-2})	a-v O$_2$ difference (ml$\cdot$100 ml^{-1})	Peak $\dot{V}O_2$ (litres$\cdot$min$^{-1}\cdot$ kg^{-1})	Peak $\dot{V}O_2$ (litres$\cdot$ min^{-1})
Cumming [111]	F	29	11.8±3.1	46±3[†]	174±11	8.61±8.1[†]	–	–	–
	M	31	12.6±3.5	56±13	170±17	10.1±1.8	–	–	–
Rowland et al. [112]	F	24	11.7±0.5	55±9[†]	198±9	10.9±1.7[†]	12.3±1.9	40.4±5.8[†]	1.84±31
	M	25	12.0±0.4	62±9	199±11	12.3±2.2	12.2±1.7	47.1±6.1	1.98±28
Obert et al. [113] Pre-training experimental group	F	7	10.66±0.3	47±7[†]	204±5	9.4±1.4[†]	13.2±1.6	40.9±8.9[†]	–
	M	9	10.66±0.5	52±8	199±9	10.5±1.8	13.0±2.1	44.1±6.1	–
Pre-training control group	F	10	10.41±0.3	46±6[†]	202±7	9.4±1.2[†]	13.1±2.8[†]	42.4±5.6[†]	–
	M	9	10.5±0.3	49±5	202±7	9.7±0.8	15.6±1.5	51.5±6.3	–
Winsley et al. [114]	F	9	10.2±0.3	45±6	192±11	8.7±1.1	12.6±1.6[†]	–	1.23±.08[†]
	M	9	10.1±0.5	47±8	195±11	8.9±1.4	14.8±2.1	–	1.41±.18

SI = Stroke index; HR = heart rate; CI = cardiac index; a-v O$_2$ difference = arterio-venous oxygen difference; $\dot{V}O_2$ = oxygen uptake. [†] Significant differences noted.

to girls have suggested that the reduced cardiac mass in girls may be associated with reduced contractility, reduced pre-load or increased afterload [106]. All of these could result in a reduced stroke index (SI) and therefore reduced cardiac index (CI). Cardiac index has generally been found to be higher in boys than girls at maximal exercise (table 1) and in the absence of sex differences in maximal heart rate, it would appear that SI most likely accounts for this difference. Absolute maximal SI index has been reported to be between 7 and 13% less in girls than boys. When corrected for body fat, this difference was reduced to 5.2% [112], but remained nonetheless. Interestingly, the lower maximal SI index apparent in girls has not always been found to relate to left ventricular dimensions, which suggests sex differences may instead relate to other factors such as the peripheral pump, systemic vascular resistance or differing adrenergic responses [113, 115].

Evidence of cardiac re-modelling following training has provided some insight into the role systemic vascular resistance may play in SI differences between boys and girls [113]. Following 13 weeks of training, both pre-pubertal boys and girls increased LV end-diastolic diameter and left ventricular mass. However, only LV end-diastolic diameter was related to percent increase in SI. Percent increase in SI was also inversely related to systemic vascular resistance, suggestive of vascular adaptations in response to high-intensity training. Of note, the decrease in systemic vascular resistance was greater in the boys than the girls, which may account for the greater increase in maximal SI in the boys.

The vasoregulatory capacity of the arterial and arteriolar vessels manipulates peripheral resistance. When blood is effectively distributed to the working muscle, peripheral resistance is reduced, which unloads the heart improving the capacity of the heart to increase SI. This is achieved by improving the flow of blood to and through the muscle and both the vasculature and skeletal muscle pump are involved. Interestingly, no sex differences in arterial compliance have been noted in pre- and early-pubertal children [116], although the beneficial role of oestrogen in vasodilation is well established and female advantage in arterial compliance is apparent in adults [117].

The skeletal muscle pump utilises the rhythmic muscle contractions to empty the venous vessels, aiding blood muscle hyperaemia and venous return. There is scant information on the skeletal muscle pump in children, but evidence in boys suggests, like adults, the skeletal muscle pump is associated with improved CI [118, 119]. In Rowland et al.'s [119] study, arterio-venous oxygen (a-v O_2) difference, a composite index of the haematological components of oxygen delivery, remained constant during unloaded exercise suggesting the increases in muscle oxygen supply were met by the increasing blood volume. Conversely, as exercise intensity increased with loading, a-v O_2 difference increased indicating decreased effectiveness of the muscle pump in satisfying the metabolic demands of the working muscle.

Whilst some studies have found no differences in estimated a-v O_2 difference at maximal or submaximal intensities between pre-pubertal girls and boys [112, 120], there are conflicting findings. Data recently published from a thoracic impedance measure of peak CI and MRI markers of cardiac size [114] demonstrated that pre-pubertal boys had a 16.7% higher a-v O_2 difference than girls. This was the only distinguishing factor to explain the significantly higher peak $\dot{V}O_2$ in the boys compared to the girls and unlike other studies no difference in either CI or SI were apparent

at maximal exercise. It is interesting to note that a-v O_2 difference was 16% lower in the girls of the control group (table 1) in the study of Obert et al. [113]. These findings are intriguing, but confirmatory studies are needed to help understand the inconsistencies in the extant data.

Muscle Cellular Metabolism during Moderate Intensity Exercise

Characterizing muscle metabolism during exercise is extremely challenging and for a long time hampered by the need for invasive measurement of enzymatic activity. ^{31}P magnetic resonance spectroscopy (MRS) has enabled the study of high energy phosphates non-invasively in human skeletal muscle. This technique can provide an estimation of skeletal muscle metabolic activity via examination of creatine phosphate (PCr), inorganic phosphate (P_1) and intracellular pH, and has been validated in both adults and children [121, 122]. There remain methodological challenges in the paediatric population, which have been outlined by Armstrong and Fawkner [123], but the data available are providing fascinating insight into cellular metabolic processes.

Children, like adults show high correspondence between MRS determined muscle phosphocreatine (PCr) activity and the pulmonary oxygen uptake ($p\dot{V}O_2$) kinetic response [124, 125]. This implies that $p\dot{V}O_2$ kinetics also provide a marker of energy utilization at the muscular level, one which may prove very useful in understanding the interplay between cardiopulmonary and metabolic processes during exercise. More comprehensive descriptions of oxygen uptake kinetic assessments have been provided elsewhere [126] and only the salient issues related to girls' responses are summarized here. The $p\dot{V}O_2$ kinetic response is tri-phasic, but only phases II and III pertain to muscle oxygen uptake kinetics. During moderate intensity exercise, the phase II $p\dot{V}O_2$ kinetic response involves

an exponential increase in oxygen uptake toward steady state, which signifies increases in muscle $\dot{V}O_2$. The primary response is described by a time constant (τ), representing the time taken (s) to achieve 63% of the change in $p\dot{V}O_2$. The attainment of a steady state denotes phase III. At higher workloads, i.e. those above the maximal lactate steady state, the $p\dot{V}O_2$ kinetic response alters, with phase III showing a delayed increase, eventually resulting in a $p\dot{V}O_2$ value higher than predicted on the basis of exercise intensity. This 'slow component' represents an increasing inefficiency in energy turnover and negatively correlates with increases in $\dot{V}O_2$ per unit increases in work, suggesting fatigue. To ensure confidence in the kinetic parameters estimated, the level of measurement rigour needed is high [126]. Few of the available oxygen uptake kinetics studies with children provide this and as such information on girls is very limited.

There is little evidence of a sex difference in $p\dot{V}O_2$ kinetic responses during moderate intensity exercise in children [127]. Neither have sex differences been found in boys and girls for MRS determined pH, P_i to PCr ratio (P_i/PCr) or PCr kinetic time constant at either the onset or offset of moderate intensity exercise [128]. In contrast, a study of the kinetic responses to high-intensity exercise found sex differences [129]. Results showed phase II $p\dot{V}O_2$ kinetics were approximately 20% slower in pre-pubertal girls compared to boys and the relative contribution of the $p\dot{V}O_2$ slow component to the end exercise $p\dot{V}O_2$ in the girls was about 30% greater. This is suggestive of a lower tolerance of fatigue in the girls, but the mechanisms underlying this response are not yet understood. One hypothesis suggests that these differences reflect a difference between boys and girls in the energetic profiles of the recruited muscles.

Barker et al. [130] have explored high-intensity exercise responses of the quadriceps muscle using MRS in children, but showed in accord with the $p\dot{V}O_2$ kinetic work, that girls responded with a greater anaerobic metabolic contribution than boys. These findings were partly attributed to the inequalities in maturity status, with relatively immature boys compared to the girls. Maturation of the cellular anaerobic response was noted in the girls in this study, who progressed from a response that was attenuated prior to puberty, but adult-like with ensuing maturation. This was not apparent in the boys, most likely an artefact of the narrow age range of the boys (9–12 years). Generally, high-intensity work requires the recruitment of fast twitch muscle fibres that are faster and larger, with a greater glycolytic and lower oxidative capacity. As discussed earlier, there is evidence of sex differences in muscle fibre type and size which vary with age and maturation, and clearly comparison of cellular metabolism during high-intensity exercise in girls and boys who are more closely aligned in terms of maturation is something which deserves further enquiry.

To summarise, there are differences between boys and girls in the aerobic responses to exercise which cannot be accounted for solely by size. Ventilatory parameters do not appear to influence peak $\dot{V}O_2$ in pre-pubertal children, however, there is scant information on the maturation of ventilatory responses in girls. It has been suggested that peripheral factors may be more important in defining aerobic fitness than cardiac function [131], but these are poorly understood in children and in particular in girls.

Acute Responses to High-Intensity Exercise

Most sports require short-duration bursts of high-intensity effort, which are supported by high muscle energy turnover. The direct examination of muscular energetics during short-duration high-intensity exercise is complex and instead investigations have largely concentrated on mechanical output markers of short duration exercise performance. The most commonly employed tests are the Wingate cycle ergometer test (WAnT) and cycle ergometer force-velocity tests,

both eliciting markers of leg power. Wingate test values for leg peak power in girls aged 11–16 years have ranged from 260 to 542 W [132–136], whilst comparable values between 250 and 555 W have been recorded using force-velocity tests in similarly aged girls [137–140]. Mean power values from the Wingate test have ranged from 228 to 341 W in 11- to 16-year-old girls [132, 136]. It is interesting to note that neither peak nor mean power appear to be unusually high in young girls who are engaged in elite tennis, swimming or gymnastics training [141]. Higher values have been recorded for elite handball players and elite sprinters [133, 141], which could not be fully explained by age and body composition; however, when comparison was made with published values for less athletic girls, peak and mean power for these elite girl athletes were not substantially different.

Longitudinal data have shown that leg peak power increases with age in both boys and girls, but the increases in boys are greater than in girls. In a study of 7- to 18-year-olds, peak power was shown to increase by 273% in girls from 7 to 16 years of age, and then to plateau [142]. In comparison, boys showed increases of 375% over this period with no plateau at 16 years. Armstrong et al. [132] examined changes in leg peak power from 12 to 17 years of age and noted increases of 66% in girls, whilst boys increased peak power by 120% over the same period. The increases noted by Armstrong et al. [132] are similar in magnitude to those of Martin et al. [142] when the same age range is considered. Similar age-related increases in mean power have been noted, again with increases in boys almost double those of girls between the ages of 12 and 17 years [132]. Sex differences in peak leg power do not appear to emerge until about 14 years of age [141], whilst mean power is greater in boys than girls from about 13 years of age [132]. Clearly age is an important predictor of short-term power in young people. The influence of stature and mass as predictors of peak and mean power have also been established [132, 143], highlighting the need to consider both body mass and composition when assessing short-term power. De Ste Croix and colleagues [143] have shown that in addition to the effects of body mass, sum of skinfolds and age, MRI determined thigh muscle volume exerts considerable influence on young people's short-term power output. Furthermore, De Ste Croix and colleagues [143] have shown using multi-level modelling that in addition to the effects of body mass, sum of skinfolds and age, MRI-determined thigh muscle volume has a significant impact on young people's short-term power output during cycling.

There are very few data on skeletal muscle metabolism during short-duration high-intensity exercise in girls. A MRS study of pH and P_i/PCr ratio during supramaximal plantar flexion exercise in pre-pubertal and pubertal girls found that the maturational differences in pH and P_i/PCr values were not statistically significant [144]. The authors concluded that glycolytic metabolism was not maturity dependent; rather, it was dependent on muscle cross-sectional area. A more recent study of the PCr kinetics and intracellular pH response during high-intensity exercise also showed a non significant sex difference in pH. It is worthy of note that in both studies [144, 145] there was considerable variability within small samples which may be masking biological significance. Wilcox et al. [145] did demonstrate that the PCr cost per watt was higher in the girls compared to the boys [145]. These findings suggest lower efficiency in the girls compared to the boys, which may be an outcome of differences in muscle fibre type, muscle activation patterns or leg vasodilatory response. However, this study failed to demonstrate that the differences in the slow component of the PCr response between children and adults were statistically significant, raising doubt that age-related change in muscle fibre recruitment substantially influences skeletal muscle metabolism during high-intensity exercise.

Does Intensive Training Pose a Threat to the Development and Health of Young Girls?

Growth

Many young athletes begin formal training before 10 years of age, with young elite gymnasts, swimmers and tennis players entering their respective sport between the ages of 6 and 7.5 years [146]. In a number of countries young girls are recruited into specialised sport schools as young as 5 years of age [147]. These elite young athletes train intensively all year round, for many hours, with weekly training volumes of 24 h not being unusual [148]. Whether intensive training such as this distorts normal growth and maturation remains a topic of much debate [7, 149].

Evidence of reduced or delayed growth in some young athletes, such as gymnasts, has been suggested to be a direct outcome of the intensive training these youngsters have endured [5, 50, 151]. Counter-argument contends that growth reductions or delay in young athletes simply reflect their late maturation [136, 152–154]. The Training of Young Athletes (TOYA) study found that elite young female swimmers and tennis players were generally taller than the general population throughout the growth period (close to the 75th percentile for stature), whilst gymnasts were generally smaller (below the 50th percentile for stature) from 10 to 17 years of age [146]. What was noteworthy was that by 18 years of age, the gymnasts were above the 50th percentile for stature and when aligned by biological age (years from attainment of menarche), gymnasts, swimmers and tennis players showed no significant differences in height. The catch-up growth noted in the gymnasts was indicative of late maturation and apparent in girls who are not involved in competitive training, but who mature late. Both the fathers and mothers of gymnasts have been found to be significantly shorter than the parents of other athletes and genetic predisposition for stature has been not only been shown to be preserved, but often

exceeded [146, 155]. Combined, this evidence indicates that the tendency for short stature in gymnasts is not, as argued by some [151], evidence of a training-induced alteration in growth, but more likely a reflection of a genetic predisposition for later development and short stature.

Reproductive Health

Menstrual dysfunction in young athletes has also been interpreted as evidence that intensive training in young girls is harmful to reproductive health [156]. Menstrual dysfunction includes delayed menarche (onset after 16 years), luteal phase defects, oligomenorrhea and amenorrhea (table 2). Several studies have concluded that female gymnasts, swimmers and ballet dancers have delayed menarche. De Ridder et al. [29] observed that, in comparison to a control group of girls matched for maturation and fatness, girls involved in competitive gymnastics exhibited delayed menarche. An early hypothesis suggested that because these young girls had low levels of body fat they did not attain a critical level of body fat (22%) necessary for menstruation. The wide variability noted in body fat at menarche [35] has provided proof that a threshold of 22% body fat is incorrect. Additionally, there is sufficient experimental evidence in women to show that it is not body fat but caloric deprivation that affects reproductive health [157].

Genetic predisposition for late menarche in athletes has also been explored. When age of menarche in a group of elite gymnasts was correlated with maternal menarchal age, it was, on average, in lag by 0.81 years [158]. This lag was double that noted for elite swimmers and triple that for elite tennis players. These data suggest that despite a genetic predisposition for delayed menarche, this does not fully explain the extent of the delay, signalling that training may indeed delay menarche in gymnasts. However, Baxter-Jones et al. [158] went on to show that when the time period between menarchal age and retirement from the sport were

Table 2. Components of the female athlete triad, diagnosis and prevention

Component of the triad	Diagnosis	Warning signs	Prevention
Energy availability [160]	Energy availability is defined as energy intake minus exercise energy expenditure, with a threshold of 30 kcal·kg^{-1} LBM·day^{-1}.	Low body mass (>85% of ideal body mass for stature). Fatigue.	Monitor dietary intake. Monitor training volume. Focus on healthy eating and caloric balance. Educate youngsters about nutritional fads. Reinforce message that body mass is only one aspect of good performance. Educational information on nutrition and energy expenditure, e.g. http://kidshealth.org/teen/food/sports/triad.html
Eating disorders [173]	*Anorexia nervosa* Refusal to maintain body mass over a minimally normal mass for age and stature. Intense fear of gaining mass or becoming fat. Disturbed body image. Secondary amenorrhea. *Bulimia nervosa* Recurrent episodes of binge eating (eating a large amount of food in a discrete period of time and lacking control over eating during the episode). Recurrent inappropriate compensatory behaviour such as self-induced vomiting, laxatives or excessive exercise. The binge-eating and purging behaviours occur at least twice a week for 3 months.	*Anorexia* Dramatic loss in body mass. Preoccupation with food, calories and body mass. Wears baggy clothes. Fine, downy facial hair. Mood swings. Avoidance of food-related social activities. *Bulimia* Noticeable loss in body mass. Excessive worry over weight. Bathroom visits after eating. Depression. Strict dieting followed by binging. Dental erosion.	Promote healthy body image. Removal of body mass/fat monitoring by coaches. Provide opportunities for developing self-coping strategies. Deemphasize body mass and thinness. Provide opportunities for nutritional counselling.
Menstrual dysfunction [174]	Oligomenorrhea – irregular menses (length between cycles >35 days). Primary amenorrhea – absence of menstruation by 15 years in girls with secondary sexual characteristics. Secondary amenorrhea- absence of menstrual cycles for 3 cycles after onset of menses.	Irregular or absent menstrual cycle.	Ask athletes to keep a training diary and include monitoring of menstrual cycle. Help girls understand that secondary amenorrhea is not normal. Provide education on reproductive health and the link between menstruation and bone health. Provide dietary education and help girls understand the link between diet and reproductive health.

Table 2. Continued

Component of the triad	Diagnosis	Warning signs	Prevention
	Luteal phase dysfunction – shortened secretory phase of the menstrual cycle, typically less than 10 days.		
Low bone mineral density [175]	If comparison with age, gender, stature and race specific Z-scores yields values ≤2.0 this is classified as a low bone mineral density for chronological age. Osteoporosis is diagnosed if low BMD for chronological age is accompanied by one or more of the following fracture histories: long bone fracture of the lower extremities; vertebral compression fracture and two or more long–bone fractures of the upper extremities.	Secondary amenorrhea. Stress fracture. History of fractures.	Provide educational information on osteoporosis. Provide information on nutrition for bone health, particularly focusing on calcium-rich foods. Monitor diet and provide opportunities for nutritional counselling.

considered, 92% of the girls began menarche prior to retiring. The authors concluded that training was therefore unlikely to cause the delay in menarche noted in the gymnasts, instead there was simply a chronological age difference in the timing of events. It would appear that exercise training, without other predisposing factors, is unlikely to be the cause of menstrual dysfunction.

The Female Athlete Triad

The female athlete triad was established in the early 1990s as a syndrome of three separate, but inter-related conditions, namely menstrual dysfunction, disordered eating and premature osteoporosis [159]. An updated position statement from the American College of Sports Medicine (ACSM) has revised the definition of the triad as the presence of one or more of (1) low energy availability (with or without eating disorders), (2) amenorrhea, and (3) osteoporosis (table 2) [160]. Prevalence estimates of components of the female triad are very dependent on the athletic group studied, with higher rates in sports where low body mass is the norm. For instance, 25% of young women in endurance, weight class or aesthetic sports had clinical eating disorders, compared to 9% of the general population [161]. Secondary amenorrhea has been reported to be as high as 69% in dancers and less than 1% in the general population [162, 163]. Osteoporosis has been found in about 13% of female athletes, although this is not too different from the normal population [164] and in pre-menopausal women low bone mineral density for age is a more appropriate marker than osteoporosis.

Much of the available data on the female triad is on college-age or young adult athletes, with few reports targeting adolescents. Two key studies of

high school athletes have shown a considerable number of girls present with components of the female triad. In a study of 170 13- to 18-year-olds, 18% had disordered eating, 24% had oligomenorrhea or amenorrhea and 22% had low bone mass for their age based on WHO diagnostic criteria [165]. A higher rate of occurrence of low energy availability (55%) was noted in a study of 80 similarly aged young athletes, with 16% diagnosed with amenorrhea and using the same WHO diagnostic criteria, 16% presented with low bone mineral density [166]. The existence of the female athlete triad in these young girls is particularly worrying given this is a time when substantial amounts of bone should be accrued.

Energy deficiency appears to be particularly harmful when combined with excessive exercise, and leads to reduced oestrogen levels, athletic amenorrhea and bone demineralisation. Loucks et al. [167] have shown that there is an energy availability threshold of 20–25 kcal $\bullet$ kg^{-1} LBM $\bullet$ day^{-1}, below which skeletal and reproductive health is compromised. This group conducted a number of studies in which women underwent energy availability manipulations, decreasing energy availability from 45 to 20 kcal $\bullet$ kg^{-1} LBM $\bullet$ day^{-1} or from 45 to 10 kcal $\bullet$ kg^{-1} LBM $\bullet$ day^{-1}. These reductions caused blunting of LH pulsatility [168] and a de-linking of bone resorption and formation [169]. The existence of an energy availability threshold may help to explain why not all athletes develop athletic amenorrhea even when following the same training programme and provides a useful marker for nutritional health.

Recent conjecture that the triad is a 'myth' [8] has caused intense debate [164, 170, 171]. This contention stems from a number of criticisms, including flaws in the epidemiological evidence, assumptions that low energy availability implies disordered eating and a lack of experimental evidence in athletes. Much of the epidemiological evidence of the prevalence of the female triad is for individual components of the triad, rather than for the synchronous appearance of all three which, it has been argued, over-inflates the extent of the problems. When occurrence of all three components is examined, prevalence falls dramatically [172]. On the other hand, the definition of the female athlete triad states explicitly that presence of one component is sufficient for diagnosis and the revised guidelines provided by the ACSM, have removed disordered eating and replaced it with energy availability, accepting that low energy availability does not equate to a pathological eating disorder [160].

Definitive conclusions on whether elite participation causes aberrations to skeletal and reproductive health are not possible. Nevertheless, there is clear evidence of a boundary between healthy and unhealthy levels of exertion when coupled with caloric limitation. Exposure to excessive training and caloric limitation causes abnormality in skeletal and reproductive function and regardless of the magnitude of the problem, young girl athletes deserve protection. Protection likely entails athlete education, coach recognition of the triad and the monitoring of both training volume and nutritional health in young elite girls. Table 2 provides an overview of the components of the triad, with possible prevention strategies for young athletes, coaches and parents.

Conclusions

Girls have differential growth and development in comparison to boys, resulting in substantial differences in body size and composition. Whilst stronger and leaner than many of her non-athletic peers, the smaller stature, shorter legs, lower muscularity and greater relative fatness of the elite girl athlete means she is not as strong, nor as fast as her male counterpart. Some discordant responses to exercise are not solely explained by body size and/or composition and there is evidence of underlying qualitative differences which require further clarification.

A young girl's involvement in elite sport predisposes her to increased risk of skeletal and reproductive health problems, particularly in sports where intense training is coupled with the need for leanness. Ensuring girls involved in elite training are in an environment which optimises their athletic potential while minimising risk is a priority. This entails sufficient knowledge of the physiologic responses to exercise in girls, as well as thorough understanding of the female triad disorder, its aetiology and prevention. Despite the burgeoning literature in the field of paediatric exercise physiology, an integrative understanding of girls' physiological responses to exercise remains elusive. Traditional technologies have proved inadequate in providing a detailed understanding of the complexity of the cellular metabolic response to exercise and this is compounded by the need to separate qualitative changes from changes which are an artefact of a growing, maturing body. More recent application of non-invasive imaging techniques and breath-by-breath gas analysis is facilitating a more integrated understanding of the responses to exercise, but the number of studies to date with girls is woefully small. In addition, more needs to be learnt about the female triad and its antecedents in younger girls. The dearth of information on girls and emergence and availability of new technologies provides plenty of scope for future studies in paediatric exercise physiology.

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